PATENT
Customer No. 22,852
Attorney Docket No. 08702.0006-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Michael Eppihimer, et al.	)	Group Art Unit: 1644
	)	
Serial No.: 09/825,580	)	Examiner: GAMBEL, P.
	)	
Filed: April 2, 2001	)	Confirmation No.: 9952
	)	
For: INHIBITION OF THROMBOSIS BY TREATMENT WITH P-SELECTIN ANTAGONISTS	)	

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

A Pre-Appeal Brief Conference is requested in this application in accordance with the USPTO Notice dated June 20, 2005.

Claims 1-20, 25-27, 31-40, 45, and 50-57 are pending in this application and are currently rejected. Claims 21-24, 28, 41, and 42 are cancelled, while claims 29, 30, 43, 44, and 46-49 are withdrawn.

I. Inherent Anticipation Rejection

Clear error is present in the rejection of claims 1-4, 8-13, 16-18, 25-27, 45-47, and 50-53 under 35 U.S.C. § 102(e) as inherently anticipated by U.S. Patent No. 5,464,778 ("Cummings") as evidenced by THE MERCK MANUAL OF DIAGNOSIS AND THERAPY 1655 (17th ed. 1999) ("Merck Manual") and Lip et al., "Hypertension and the

prothrombotic state," J. Hum. Hyper. 14: 687-90 (2000) ("Lip"). Claim 1, which includes the limitation "in a subject having hypertension" is representative of the rejected claims:

> 1. A method of treating or inhibiting thrombosis in a subject having hypertension comprising administering to the subject a composition comprising an effective amount of a PSGL-1 protein having a P-selectin ligand activity chosen from at least one of:
>
> a) inhibiting P-selectin or E-selectin binding;
>
> b) inhibiting adhesion of at least one of leukocytes to endothelial cells, leukocytes to platelets, leukocytes to blood vessels, and platelets to blood vessels;
>
> c) inhibiting leukocyte recruitment to platelets and endothelial cells;
>
> d) increasing leukocyte migration;
>
> (e) increasing movement of at least one of leukocytes and platelets relative to blood vessels; and
>
> f) increasing leukocyte rolling velocity.

The Office asserts that Cummings inherently discloses treatment of the medical conditions of the instant claims. The Office cites the Merck Manual and Lip to support its argument that the claimed methods are inherently anticipated. These arguments are factually and legally insufficient for a finding of inherent anticipation.

To find inherent anticipation the reference "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference." MPEP § 2112 (citing *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1376 (Fed. Cir. 2003)) (emphasis added). Inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." MPEP § 2112 (citing *In re Robertson*, 169 F.3d 743,

745 (Fed. Cir. 1999)) (emphasis added). Finally, the Office must "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." MPEP § 2112 (citing *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)) (emphasis added).

Hypertension is not necessarily present in the medical conditions described in Cummings. The Merck Manual does not state that hypertension is necessarily present whenever a patient suffers from a condition disclosed in Cummings. Rather, the Merck Manual describes hypertension as a risk factor that may contribute to various medical conditions. Similarly, Lip merely describes an association between hypertension and certain medical conditions, but does not state that hypertension is necessarily present in those conditions. Moreover, as indicated in the Declaration filed with Applicants' response of September 13, 2006, it is known to those of skill in the art that hypertension is not always present in patients suffering from the conditions of Cummings. At best, the Merck Manual and Lip indicate that the conditions of Cummings and hypertension may co-exist, but they do not show that hypertension is necessarily present in the conditions of Cummings or that the treatment of thromboses in patients suffering from hypertension necessarily flows from their teachings. Accordingly, these references fail to factually or legally support a finding of inherent anticipation.

II. Obviousness Rejections

Clear error is present in the rejection of claims 1-20, 25-27, 31-40, 45, and 50-57 under 35 U.S.C.§ 103(a) as unpatentable over Cummings and Larsen et al., U.S. Patent

No. 5,840,679 ("Larsen") in view of Blann et al., "Evidence of platelet activation in hypertension," J. Hum. Hyper. 11:607-609 (1997) ("Blann"), Araneo et al., U.S. Patent No. 6,150,348 ("Araneo") and DeFrees et al., U.S. Patent No. 5,604,207 ("DeFrees"), and further in view of the Merck Manual.

The Office apparently contends that the claimed methods are obvious because administration of PSGL-1 to treat the conditions recited in Cummings and Larsen would inherently treat a patient with hypertension. However, the Office continues to rely on an improper finding of inherency and the obviousness rejection is improper.

A proper prima facie obviousness rejection requires some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Additionally, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. See M.P.E.P. § 2143.

The Office has failed to establish prima facie obviousness because the combination of the cited references fails to teach or suggest the claimed method and fails to provide the motivation to combine references. Cummings and Larsen neither teach nor suggest the use of a PSGL-1 protein for treating or inhibiting thrombosis in a patient with hypertension. As noted above, Cummings neither teaches nor suggests that hypertension is necessarily associated with any of the conditions discussed therein, and the absence of a necessary association is known to those of skill in the art. Larson, Blann, Araneo, Defrees and the Merck Manual also fail to show such a necessary association. Therefore, the cited references fail to teach or suggest all of the claim

limitations, and in the absence of such a teaching, one of skill in the art would have no motivation to arrive at the claimed invention by combining references. Accordingly, the publications cited by the Office fail to support prima facie obviousness of the claimed methods.

III. Rejection of claim 27

There is clear error in the rejection of claim 27 under 35 U.S.C.§ 103(a) as unpatentable over Cummings and Larsen, in view of Blann, Araneo, DeFrees, the Merck Manual, and further in view of Maugeri et al., "Polymorphonuclear Leukocyte-Platelet Interaction: Role of P-selectin in Thromboxane B2 and Leukotriene C4 Cooperative Synthesis," Thromb. Haem. 72:450-456 (1994) ("Maugeri") and Johnston et al., "Differential Roles of Selectins and the α4-Integrin in Acute, Subacute, and Chronic Leukocyte Recruitment In Vivo," J. Immunol. 159:4514-4523 (1997) ("Johnston"). Claim 27 is directed to a method for inhibiting thrombus formation induced by leukotriene C_4 ("LTC_4") in a subject by identifying a subject at risk of thrombosis resulting from hypertension and administering to the subject a composition comprising an effective amount of soluble PSGL-1 protein or a fragment thereof.

The Office asserts that LTC_4 was a known thrombus-inducing agent involved in thrombus formation and thrombotic conditions, as allegedly shown by Maugeri and Johnston, and concludes that the claimed method is obvious. Again, the Office relies on an improper finding of inherency and the obviousness rejection is improper.

As noted above, neither Larsen nor Cummings teach or suggest treating or inhibiting thrombosis in a subject with hypertension and Blann, Araneo, DeFrees and the Merck Manual fail to compensate for this deficiency. None of these references

discuss administering a PSGL-1 protein for treating or inhibiting thrombosis in a subject having hypertension, and do not indicate that hypertension is necessarily present in the disclosed conditions. Neither Maugeri nor Johnston compensate for these deficiencies because they also fail to discuss treating or preventing thrombosis in a subject having hypertension using a P-selectin ligand protein. To one of skill in the art, Maugeri and Johnston would not render the claimed invention obvious and the rejection of claim 27 is improper.

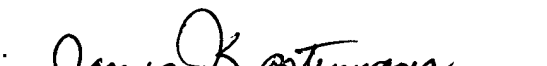
Applicants request withdrawal of all outstanding rejections and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this request and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 28, 2006

By: 
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